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14. ABSTRACT: This study involves the technical development and clinical testing of a novel technique for magnetic resonance imaging (MRI) guided prostate biopsy in a 1.5T horizontal bore scanner using a dedicated interventional table. We primarily hypothesize that the integration of diagnostic and interventional MRI enables needle biopsy targeting to foci of tumor recurrence after radiotherapy, and will enable a determination of the diagnostic accuracy of MRI in mapping sub-sites of tumor recurrence after radiotherapy. Major finding to date: This clinical study received ethics approval from USAMRMC approval on October 13 2006. Funds were released after HSRRB approval, and received in September 2006. In the first year of research, 14 patients have been accrued to stage 1 (phase 1) of the trial. We will proceed to Stage 2 as soon as we receive HSRRB approval of study amendment. Tasks 1a-1d are complete, as per the Statement of work.					
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INTRODUCTION:

This study involves the technical development and clinical testing of a novel technique for magnetic resonance imaging (MRI) guided prostate biopsy in a 1.5T horizontal bore scanner using a dedicated interventional table. We primarily hypothesize that the integration of diagnostic and interventional MRI enables needle biopsy targeting to foci of tumor recurrence after radiotherapy, and will enable a determination of the diagnostic accuracy of MRI in mapping sub-sites of tumor recurrence after radiotherapy.

This study will enroll up to 50 patients with suspicion of locally recurrent prostate cancer after external beam radiotherapy in a pilot, three-stage trial design. The first stage will include technical development and optimization of the imaging technique. The second stage will include technical development of optimization of the biopsy technique, followed by a clinical evaluation stage. This preliminary data will be critical for the judicious conduct of a subsequent phase I-II trial.

BODY:

USAMRMC approval for the conduct of this study was obtained on October 13 2006, therefore the statement of work has been delayed by one year for regulatory approval.

We therefore report Year 1 of the Statement of work, Specifically Aim 1, and Tasks 1a-1d.

Aim 1: To test the hypothesis that stereotactic MRI-guided prostate needle biopsies can be performed with improved anatomic targeting accuracy and tolerability when patients are positioned supine in a conventional MR scanner. To test this hypothesis we plan:

Task 1a. To design a custom interventional MRI table and hardware system that provides immobilization and perineal access in the supine position. The proposed table design will incorporate the following features: 1) an open panel for perineal exposure and to create operative space, 2) supports for hip and knee flexion and immobilization, and 3) hardware attachments sites for the transperineal template.

Deliverable: A custom MRI table for pelvic interventions.

Progress: The prototype table has been designed, constructed, and tested. Pictures are provided in Appendix.

Task 1b. To measure prostate motion while patients are immobilized on the custom table and compare results with prone or lateral positioning. Ten healthy volunteers will be enrolled on an IRB/HSRBB approved protocol. Prostate motion will be measured while immobilized on the interventional MRI table using sagittal and axial, single-slice cinematic MRI. The MR coordinates of three reproducible points within the prostate gland will be documented, and their displacement within the coordinate system will be calculated and described with the mean and maximum vector distance for each volunteer. This data will also be acquired in the prone and lateral decubitus interventional positions. Mean displacements will be compared using a Student's T statistic.

Justification for sample size: Estimating a mean displacement of 0.3 ± 0.2 mm in the supine position, and 1.4 ± 0.5 mm in the prone position due to respiratory motion, we project a required sample size of 6 patients to detect a difference in the mean displacement of the prostate ($\alpha=0.05$, $\beta=0.8$, single sided t-test). Ten healthy volunteers will therefore be sufficient to address this task.

Deliverable: Demonstration that the prostate gland is more stable in the supine interventional position, providing evidence in support of improved anatomic targeting accuracy with this approach.

Progress: Due to delays in regulatory approval (Health Canada) of the intra-rectal device, only 6 subjects have usable data for prostate motion analysis, and 4 have been analyzed to date. Results to date confirm minimal respiratory motion of the prostate in the supine position

Patient	Mean A/P Motion (mm)	Mean S/I Motion (mm)
1	0.16 +/- 0.21	0.25 +/- 0.22
2	0.20 +/- 0.17	0.29 +/- 0.34
3	0.16 +/- 0.22	0.21 +/- 0.12
4	0.12 +/- 0.12	0.013 +/- 0.29

Task 1c. To measure patient comfort while immobilized on the custom table and compare results with those of prone and lateral positioning. With each MRI scan described in 1b, volunteers will be asked to rate the level of positional discomfort on a standard 10-point visual analog scale. We expect that these results, and those obtained in *Task 1b*, will provide strong justification for the adoption of the supine interventional approach for all subsequent work.

Deliverable: Demonstration of improved patient comfort in the supine position

Progress: All patients tolerated positioning and imaging procedures well. One patient had imaging terminated after 45 minutes due to rectal discomfort with the intra-rectal coil. All other patients completed imaging procedures without complications. Patient self-reported minimal discomfort mainly due to being confined in the MRI scanner for the duration of imaging. There were no reports of musculoskeletal discomfort.

Task 1d. To confirm the geometric needle targeting accuracy of the supine trans-perineal system in a gel phantom. Using a water-based gelatin phantom with a penetrable membrane, biopsy needles will be inserted through the template at predetermined depths. The actual location of the needle tip signal void on biopsy verification imaging will be compared to the projected location. The vector distance between these two points represents the geometric needle targeting accuracy of the system. The spatial accuracy of MR images, corrected for gradient non-linearity, will be verified in phantom studies.

Deliverable: Demonstration that a mean geometric targeting accuracy of 2mm is maintained with supine orientation of the system.

Progress: A phantom experiment was conducted using Aegis targeting software, and Prostate Phantom (Model 053, CIRS Inc.), as well as Invivo 16 gage automatic biopsy gun. Needle targeting accuracy (n=7) was: X=0.34+/- 0.31 mm, Y=-1.57+/-1.09 mm, Z= 2.28 +/- 4.05 mm. Greater error in the z dimension is due to uncertainties in insertions depths due to 1cm incremental marking on the commercial needle. Targeting accuracy compares well with comparable techniques published in the literature.



KEY RESEARCH ACCOMPLISHMENTS:

- Prototype dedicated interventional table.
- Demonstrated prostate immobilization and comfort
- Demonstrated needle targeting accuracy of the system
- Ready to proceed to stage 2 of the trial

REPORTABLE OUTCOMES: n/a

CONCLUSION: The statement of work has been delayed by one year for regulatory approval, and work to date has met projected deliverables for year 1.

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APPENDICES: ISMRM Abstract (Reference 1)

A System for Prostate Intervention in a 1.5 T MRI Scanner in the Supine Position

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Introduction: Prostate cancer is the most likely cancer to develop in a Canadian male with a prevalence of 1 in 7.1 cases in 2005 [1]. In the United States 230,000 new cases of prostate cancer have been projected for 2005 [2]. Despite improvements in the delivery and reduction in associated toxicity of external beam radiotherapy, local persistence or recurrence of disease remains prevalent in 25-51% of patients [3,4]. A careful and thorough investigation of the spatial distribution of cancer within the prostate gland is paramount to meaningful progress in effective prospective management and therapy. Magnetic Resonance Imaging (MRI) provides the ability to deliver excellent soft tissue contrast and resolution of the anatomy. It also provides an opportunity to spatially characterize pathology and biology through dynamic contrast-enhanced (DCE) imaging, MR spectroscopic imaging of tissue metabolites, and diffusion-weighted (DWI) imaging. Previous systems have been developed for prostate interventions in a standard 1.5 T MRI scanner with excellent biopsy-needle targeting accuracy, but have required the patient to be placed in the prone or left lateral decubitus position [3], thereby compromising stability, patient comfort, and safety. A number of recent studies have shown that prostate motion is greatly reduced when patients are placed in the supine position due to greater patient comfort and reduced respiratory motion [4-6]. In this work, the feasibility of creating adequate perineal exposure for prostate interventions in the supine position using dedicated table architecture is investigated.



Figure 1: Picture of the custom imaging table for patient positioning in the supine position docked to GE 1.5 T MRI scanner.



Figure 2: Image showing the accessibility of the perineum and accommodation of stereotactic perineal template and coil.

Materials/Methods: To permit the patient to be positioned supine and allow access to the perineum, a dedicated prostate interventional table (Figure 1) was designed in collaboration with Sentinelle Medical Inc. (Toronto, Canada). The table is a modification of Sentinelle Medical's Vanguard System which is used in breast imaging and intervention. The table has been revised to provide boot supports for hip and knee flexion and immobilization, pelvic immobilization, imaging coil integration, and ample room for perineal exposure and operative space (Figure 2). The table has also been designed to accommodate both the "access to prostate tissue under MRI guidance" (APT-MRI) device [7,8] as well as a stereotactic perineal template and coil system [3]. The interventional table provides ease of mobility between the MRI suite and adjacent rooms. Patients can then be set-up on the table prior to it being docked to the MRI scanner, thus freeing the unit for standard clinical workflow. An REB/HSRBB approved protocol is currently enrolling patients to develop the revised interventional techniques and measure organ motion and patient comfort in the new system. Prostate motion was measured using a 2D FIESTA with fat saturation (TE/TR – 1.9/6.2ms; matrix 320x224, FOV 26 cm, 8mm slice thickness) and temporal resolution 2sec, and analyzed with manual POI tracking using MIPAV software (Medical Image Processing Analysis and Visualization – NIH).

Results: On an initial trial, the patient was placed on the table and imaged for a period of 60 minutes with the endorectal coil in place. There was no report of discomfort from the patient, and perineal exposure was excellent (Figure 2). Respiratory and peristaltic motion observed during the 2D FIESTA sequence caused negligible movement of the prostate gland. Maximum displacement of the prostate gland was 0.51mm and 1.02mm, associated with a mean displacement of 0.00 +/-0.31mm and 0.00 +/-0.46mm in the AP and SI directions, respectively, over 2 minutes of imaging time.

Conclusions: This system for prostate intervention provides a means by which MRI data can be used to accurately guide and provide feedback to validate new imaging techniques with the patient placed in the supine position, thereby minimizing patient discomfort and prostate motion.

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